### (19) World Intellectual Property **Organization**

International Bureau



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(43) International Publication Date 8 July 2004 (08.07.2004)

PCT

#### (10) International Publication Number WO 2004/056860 A3

- (51) International Patent Classification7: C07K 14/575, C12N 15/00, A61K 38/00
- (21) International Application Number:

PCT/GB2003/005605

(22) International Filing Date:

22 December 2003 (22.12.2003)

(25) Filing Language:

English

(26) Publication Language:

English

(30) Priority Data: 0229856.0

20 December 2002 (20.12.2002) GB

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- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU. SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA. UG, US, UZ, VC, VN, YU, ZA, ZM, ZW.
- (84) Designated States (regional): ARIPO patent (BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

#### Published:

- with international search report
- before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments
- (88) Date of publication of the international search report: 13 January 2005

[Continued on next page]

В

#### (54) Title: CHORIONIC SOMATOMAMMOTROPIN HORMONE SPLICE VARIANTS

QUERY: 1 MAGSRISILLANALICIPALQRAGAVQIVPLSHIANIQAHRAHQLAIDTYQKFVSS 60 HAACSRYSLLIAFALLCLPHLQBAGAVQTVPLSRLPDHAHLQAHRAHOLAIDTYOBF +

SBJCT: 1 MAAGSRISLLLAPALLCLIMIQUAGAVQIVFLSRLFDHAMIQAMBAHOLAIDTYOEFERT 60

------GEDSIPPPSENESTOQUESELELIRISLLLIESALEPVRPIR 102 DSIPTPSISSEETOCESHLELLRISLLA.IRSM.ZPVRVI.R SBICT: 61 YIPKOQXYSYLHOSQTSPCFSUSIPYPSREREYOOKSBLEELRISELLIKSBLEPVRPLE 120

CHAT: 103 SEPANDLAVIOTSDSDOYHLANDLEDGIQTLACRLEDGSRRTGQILKOTYSKFD/HSENED 162

SAPARELY/D7SDS/DYHLLADLREGIOTI MERLEDSSRFTG011&07/58/P079SH000

SAICT: 121 SMFAXHAVIDTSDSIDTHLLADLERGIQTAGGLEGGSRATGQILAQTYSAFDTHSHHED 180

QUERY: 163 ALLICATGLLYCPRIDNOXVETPLEHVQCRSVEGSOGF 199 ALLANYGLLYCPRODOCVETFLERYOCRSVEGSCG SECT: 181 ALLENGLLYCPRADEDEVETPLEHVOCRSVEGSCEP 217 QUERY: 1 MAPGERTELLIAPALICEPHIQEAGAVOTVPLERLFDBANDOMPRABOLAIDTYDEFVES 60 KAPGSRTSILLAPALLCLFNLOEAGAVOTVPLSKLFDRANLOARRAHOLAIDTYORF

SBUCT: 1 HAPCSRTSLLLAFALLCLPHIQEAGAVQTVPLSRLPDHAMLQAHRAHQLAIDTYQEPEBT 60

OUERY: 61 W-----GERSIPTPSEMEETOOKSULRILRISLILIRSMIRPVRFIR 102 DSIPPPSIMERTOOKSHUKLIRISLLLIRSMURPVIPILE

SBICT: 61 YEPKOOKYSFLEDSOTSPCFSDSIPTPSPACETOOKSBLEEJRISIJALTESPLEPVRPLR 120 \*

QUEXY: 103 SEYANNLYYDTSDSDDYHLLEDLEDGIQTLWGRLEDGSRRYGOILEOTYSEYDTNSHNED 162 SUPANILWYD7SDSDDYKLLADLERGIO7LAGRLEDGSRRTGOLLADTYSKFDTWSHNRD

SBJC7: 121 SMFARMLVYDTSDSDDYHLLKDLERGIQFLACTRLEDGSRRFGQILKQTYSKFDFRSHRHD 180

QUERY: 163 ALLASYGLLYCPEKDROXYSTYLRIAVOCRSVEGSCEF 199 ALLEHYGLLYCYEKINDRVETPLRHVOCRSVEGSCGI

SEJET: 181 ALLANYGILLYCPRUBURVETFLANVOCKSVEGSOGP 217

(57) Abstract: The invention is based on the discovery that the INSP100 is a novel splice variant of human chorionic somatomammotropin hormone 2 (HCS-B; Q14407) and that INSP104 is a novel splice variant of human Chorionic somatomammotropin hormone 1 (hCS-A;P01243).



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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

International Application No PCT/GR 03/05605

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According to	o International Patent Classification (IPC) or to both national classific	ation and IPC						
	SEARCHED							
Minimum documentation searched (classification system followed by classification symbols)  IPC 7 C07K								
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched								
Electronic data base consulted during the International search (name of data base and, where practical, search terms used)  EPO-Internal, Sequence Search, BIOSIS, PAJ, FSTA, EMBASE, WPI Data								
	ENTS CONSIDERED TO BE RELEVANT							
Category °	Citation of document, with indication, where appropriate, of the re-	evant passages	Relevant to claim No.					
X	DATABASE UniProt 'Online!  1 November 1996 (1996-11-01), "CI somatomammotropin CS-5."  XP002304199  retrieved from EBI accession no. UNIPROT:014406  Database accession no. Q14406 the whole document  -& VNENCAK-JONES C L ET AL: "HOTFOR GROWTH HORMONE GENE DELETIONS HOMOLOGOUS REGIONS OUTSIDE OF ALL SCIENCE, AMERICAN ASSOCIATION FOR ADVANCEMENT OF SCIENCE, US, vol. 250, 21 December 1990 (1990-pages 1745-1748, XP002044349 ISSN: 0036-8075	T SPOTS S IN J REPEATS" R THE	1-45					
<u> </u>	ner documents are listed in the continuation of box C.	Patent family members are liste	d in annex.					
considered to be of particular relevance  "E" earlier document but published on or after the international filling date  "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)  "O" document referring to an oral disclosure, use, exhibition or other means  "P" document published prior to the international filling date but		"T" later document published after the International filling date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention  "X" document of particular relevance; the claimed invention cannot be considered novel or carnot be considered to involve an inventive step when the document is taken alone  "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.  "&" document member of the same patent family  Date of mailing of the international search report						
15 November 2004		01/12/2004						
Name and n	nailing address of the ISA  European Patent Office, P.B. 5818 Patentlaan 2  NL - 2280 HV Rijswijk  Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  Fax: (+31-70) 340-3016	Authorized officer  Turri, M						

Inte al Application No PCT/GB 03/05605

C (C1	gion) DOCUMENTS CONSIDER	PCT/GB 03/05605	
Category °	Citation of document, with Indicates when a second of the		
Jalegory	Citation of document, with Indication, where appropriate, of the relevant passages	Relevant to claim No.	
Α	CHEN E Y ET AL: "THE HUMAN GROWTH HORMONE LOCUS: NUCLEOTIDE SEQUENCE, BIOLOGY, AND EVOLUTION" GENOMICS, ACADEMIC PRESS, SAN DIEGO, US, vol. 4, no. 4, 1989, pages 479-497, XP000990095 ISSN: 0888-7543 -& DATABASE GENEBANK 8 November 1994 (1994-11-08), CHEN E Y ET AL: "HUMAN GROWTH HORMONE (GH-1 AND GH-2) AND CHORIONIC SOMATOMAMMOTROPIN (CS-1, CS-2 AND CS-5) GENES, COMPLETE CDS" XP002185150 retrieved from GENEBANK Database accession no. J03071 the whole document		
A	HIRT H ET AL: "THE HUMAN GROWTH HORMONE GENE LOCUS STRUCTURE EVOLUTION AND ALLELIC VARIATIONS" DNA (NEW YORK), vol. 6, no. 1, 1987, pages 59-70, XP009039318		
Т	ISSN: 0198-0238 -& DATABASE SWISSPROT 25 October 2004 (2004-10-25), "Chorionic somatomammotropin hormone precursor (Choriomammotropin) (Lactogen)" XP002304200 retrieved from SWISSPROT Database accession no. P01243 abstract		
A	SEEBURG P H: "THE HUMAN GROWTH HORMONE GENE FAMILY NUCLEOTIDE SEQUENCES SHOW RECENT DIVERGENCE AND PREDICT A NEW POLY PEPTIDE HORMONE"  DNA (NEW YORK), vol. 1, no. 3, 1982, pages 239-250, XP001058450 ISSN: 0198-0238		
A	LI C H ET AL: "AMINO-ACID SEQUENCE OF HUMAN CHORIONIC SOMATOMAMMOTROPIN" ARCHIVES OF BIOCHEMISTRY AND BIOPHYSICS, vol. 155, no. 1, 1973, pages 95-110, XP009039320 ISSN: 0003-9861		

Int nat Application No
I PCT/CR 03/05605

0.40		PCT/GB 03/05605	
	ation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
A	SCHNEIDER A B ET AL: "IDENTIFICATION OF THE INTER CHAIN DI SULFIDE BONDS OF DIMERIC HUMAN PLACENTAL LACTOGEN" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 254, no. 10, 1979, pages 3782-3787, XP002304196 ISSN: 0021-9258		
A	SHINE J ET AL: "Construction and analysis of recombinant DNA for human chorionic somatomammotropin." NATURE. 8 DEC 1977, vol. 270, no. 5637, 8 December 1977 (1977-12-08), pages 494-499, XP009039351 ISSN: 0028-0836		
A	SHERWOOD L M ET AL: "AMINO-ACID SEQUENCE OF HUMAN PLACENTAL LACTOGEN" NATURE NEW BIOLOGY, vol. 233, no. 36, 1971, pages 59-61, XP009039319 ISSN: 0090-0028		
A	TODA Y ET AL: "Alu elements as an aid in deciphering genome rearrangements." GENE. 31 DEC 1997, vol. 205, no. 1-2, 31 December 1997 (1997-12-31), pages 173-176, XP002304198 ISSN: 0378-1119		
P,A	STRAUSBERG R L ET AL: "Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences" PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA, NATIONAL ACADEMY OF SCIENCE. WASHINGTON, US, vol. 99, no. 26, 24 December 2002 (2002-12-24), pages 16899-16903, XP002964739 ISSN: 0027-8424		
	SELBY M J ET AL: "ANALYSIS OF A MAJOR HUMAN CHORIONIC SOMATOMAMMOTROPIN GENE EVIDENCE FOR 2 FUNCTIONAL PROMOTER ELEMENTS"  JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 259, no. 21, 1984, pages 13131-13138, XP002304204 ISSN: 0021-9258		
	(continuation of second sheet) (January 2004)		

PCT/GB 03/05605

INTERNATIONAL SEARCH REPORT	PCT/GB 03/05605	
Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.	
BARRERA-SALDANA H A ET AL: "2 STRUCTURALLY DIFFERENT GENES PRODUCE THE SAME SECRETED HUMAN PLACENTAL LACTOGEN HORMONE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 258, no. 6, 1983, pages 3787-3793, XP002304205 ISSN: 0021-9258		
BARSH G S ET AL: "The human growth hormone gene family: structure and evolution of the chromosomal locus." NUCLEIC ACIDS RESEARCH. 25 JUN 1983, vol. 11, no. 12, 25 June 1983 (1983-06-25), pages 3939-3958, XP002304206 ISSN: 0305-1048		
	BARRERA-SALDANA H A ET AL: "2 STRUCTURALLY DIFFERENT GENES PRODUCE THE SAME SECRETED HUMAN PLACENTAL LACTOGEN HORMONE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 258, no. 6, 1983, pages 3787-3793, XP002304205 ISSN: 0021-9258  BARSH G S ET AL: "The human growth hormone gene family: structure and evolution of the chromosomal locus." NUCLEIC ACIDS RESEARCH. 25 JUN 1983, vol. 11, no. 12, 25 June 1983 (1983-06-25), pages 3939-3958, XP002304206	Relevant to claim No.  BARRERA-SALDANA H A ET AL: "2 STRUCTURALLY DIFFERENT GENES PRODUCE THE SAME SECRETED HUMAN PLACENTAL LACTOGEN HORMONE" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 258, no. 6, 1983, pages 3787-3793, XP002304205 ISSN: 0021-9258  BARSH G S ET AL: "The human growth hormone gene family: structure and evolution of the chromosomal locus." NUCLEIC ACIDS RESEARCH. 25 JUN 1983, vol. 11, no. 12, 25 June 1983 (1983-06-25), pages 3939-3958, XP002304206